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United States
Department of
Agriculture

Agricultural
Research
Service

November 1984

Agricultural Biotechnologies

Strong Acceleration of Research Programs at Beltsville

United States
Department of
Agriculture

National Agricultural Library

Cover: Mapping the genes of a soybean protein. A photographic negative (background) has been exposed by radioactively labeled nucleotides that were chromatographically separated in a gel. Each bar represents a "letter," or nucleotide, in the genetic code. (0484X525—23)

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Strong Acceleration of Research Programs at Beltsville

Introduction

In a recent report to the U.S. Department of State, a panel of experts termed genetic engineering "one of four major scientific revolutions of this century, on a par with unlocking the atom, escaping the earth's gravity, and the computer revolution." Recent developments in genetic engineering and the related biotechnologies undoubtedly have important and long-lasting implications for agricultural research. Private industry has been quick to exploit these new biotechnologies for profit, and the first products from them, such as insulin and monoclonal antibodies to organisms causing calf diarrhea, are already on the market. Universities are joining with industry to establish biotechnology centers such as those at North Carolina State, Cornell, and, more recently, the University of Maryland. Foreign countries, particularly those in the European Economic Community (EEC) and Japan, are vigorously increasing their efforts in the sciences related to the agricultural biotechnologies to capture a major share, not only of the world market, but more especially of the potentially large U.S. domestic market for agricultural technologies.

Scientists and administrators in the Beltsville Area of the U.S. Department of Agriculture (USDA), Agricultural Research Service (ARS), have themselves responded to the need to emphasize the new biotechnologies, in, for example, the "Proposal for Plant Cell Culture/Genetic Engineering/Molecular Biology Research at BARC [Beltsville Agricultural Research Center] and Midatlantic SAES's [State Agricultural Experiment Stations]" of October 1981 and the prospectus "Application of Genetic Engineering to Animal Production" of 1982. In the spring of 1982, a seminar on "Bioregulation" was sponsored by the administrator of ARS, and projects derived from the seminar were subsequently funded. More recently, an increased emphasis has been placed by the Administrator on strengthening the biotechnology-related research in the Agency, particularly in the Beltsville Area. This brochure is a summary of an unpublished study[1] designed to identify the areas of biotechnology-related research that need an increase in emphasis and to describe the biotechnology-related research ongoing in the Beltsville Area.

In the Department, ARS is an agency that has responsibility for conducting research to provide technologies to solve agricultural problems. The research is conducted in 11 areas and approximately 140 locations within the United States. The Beltsville Area, the largest of the Areas, is headquartered in Beltsville, Md. It consists of the Beltsville Agricultural Research Center, the Beltsville Human Nutrition Research Center, the National Arboretum, and the Family Economics Research Group.

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[1]"Strong Acceleration of Research Programs Relevant to Agricultural Biotechnologies at Beltsville," which is available on request from the author, H.G. Purchase, chairman of biotechnology taskforce, special scientific adviser to the director, Beltsville Area, Bldg. 003, Room 224, BARC-West, Beltsville, Md. 20705.

Introduction to Biotechnology

What Is Biotechnology?

In its broadest sense, biotechnology includes the management of biological systems for the benefit of humanity. It includes all aspects of the exploitation and control of living organisms. Biotechnology was used at the dawn of civilization in making wine, cheese, and bread. Humans were unknowingly exploiting the ability of micro-organisms to convert sugar in grapejuice into alcohol in wine, to break down the proteins in milk to soften and flavor the cheese, and to convert the starch in flour into carbon dioxide, which causes bread to rise during baking. These are the bases of the definition that biotechnology is "the application of engineering and technological principles to the life sciences."[2]

To many with an industrial background and from the perspective of the Congress of the United States, biotechnology is the use of living organisms or their components in industrial processes, or it is the collection of industrial processes that involve the use of biological systems; for some industries, the processes involve the use of genetically engineered micro-organisms.[3] So modern industry has adopted many of the biotechnologies. Companies all over the world are using living organisms to produce goods and services. The organisms may be animal or plant, they may be microscopic, like the simplest forms of life, or large mammals like cattle, which are among the most complex forms of life. So, much of what we eat, drink, wear, and use in our daily lives is a product of biotechnology.

Ways Biotechnology Serves Us

1. Fermentation. Micro-organisms growing in large vats are used to produce sweeteners like high-fructose sugar; vitamins A, E, and K; organic solvents such as acetone and alcohol; and even ammonia for fertilizer.

2. Pharmaceuticals. Many antibiotics and hormones, like insulin, that help heal us when we are sick are purified from micro-organisms. There are great opportunities for production of vaccines against animal and human diseases. Substances like interferon, which is the body's first line of defense against invading disease micro-organisms, can be produced by biotechnological methods.

3. Food Processing. A gummy substance produced by a bacterium has been used for many years as a thickening agent for salad dressings, sauces, whips, toppings, processed cheeses, and dairy products. Products as diverse as sweeteners, food protein, and meat tenderizers are produced in large quantity by biotechnological methods.

4. Environment. Many rocks contain so little mineral that chemical extraction is unprofitable. However, using micro-organisms to leach minerals from rocks, while slow, is a practical process for obtaining some minerals from low-grade ores. Similarly, micro-organisms can be used to remove heavy metals from industrial effluents and to devour oil or certain pesticides.

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[2]Dictionary of Scientific and Technical Terms. S. B. Parker, ed. 3d ed. McGraw-Hill, New York. 1984.
[3]Impacts of Applied Genetics: Microorganisms, Plants and Animals. Congress of the United States, Office of Technology Assessment. U.S. Government Printing Office, Washington, D.C. 1981. 331 pp.

5. Weather. Even some of the adverse effects of weather can be modified by biotechnological methods. For example, bacteria have been engineered to fight frost by preventing ice crystals from forming on the leaves of plants.

6. Marine. Biotechnologies can be used to control diseases of economically important fish and mollusks such as clams and oysters and to help dispose of seafood-industry wastes.

7. Artificial Intelligence. Electronics has progressed greatly since Samuel Morse first sent a telegram from Washington to Baltimore and the vacuum tube led to the development of radio and television. These technologies have given way to transistors and integrated circuits, most of which are based on the element silicon. Organic molecules, with their greater complexity, will allow the development of biochips, which, in turn, will permit the development of computers an order of magnitude more sophisticated than current computers and will also advance the development of artificial intelligence.

How ARS, Beltsville Area Defines Biotechnology

Narrowing the Field

In this broad field of biotechnology, only a small part is appropriate for ARS. Staff scientists in the Agency are concerned about supplies of high-quality food and other farm products at affordable prices for Americans and for export, about the economic welfare of the U.S. agricultural enterprise, and about conserving the Nation's natural resources. In terms of biotechnology, these concerns are narrower than those of industrial organizations or even of State agricultural experiment stations.

Research in the Agriculturally Related Biotechnologies

Our research in agriculturally related biotechnologies has the following common characteristics: revealing how nature works and discovering new knowledge (not how to apply existing knowledge to field problems). Even though the results of the research may not be immediately evident, the research must be directed to eventually solving an important agricultural problem. This is the only way to be sure that we will develop new methods to improve farming. However, we can't predict whether or what results will be obtained, and therefore the research can only be planned in a very general way.

Commodities

The research will relate to many commodities and will be interdisciplinary, involving many fields of science directed at the problem simultaneously. Specific plants or animals will be used as models in the individual experiments, but the results of a specific experiment will likely tell us more about all life forms.

Research Methods

In recent years, new methods for doing research have been developed that have revolutionized the way we go about solving agricultural problems. These newly developed methods will be the bases for the research. Examples are genetic-engineering techniques that include transfer of genes from plants or animals to micro-organisms such as *E. coli* (recombinant DNA technology). To engineer genes, we must be able to identify the genetic message in organisms and determine how it is controlled. We use plant cell and tissue culture, preparation of protoplasts (cells without cell walls), protoplast fusion, growth of embryos of plants and animals in vitro, and transfer of embryos from one animal to another, and we make artificial peptide hormones, pheromones, and lymphokines (the chemical substances that cells use to communicate with one another). While the older techniques can still be used in research, they are not specifically included here in the term "biotechnology." Examples of the older, more conventional techniques excluded from this study are crossbreeding of plant and animals, preparation of vaccines by killing disease-producing organisms with heat or chemicals, and application of tests that detect and determine the amount of hormones in the blood and body fluids.

ARS Goals and Biotechnology Research

Goals

Through fundamental and applied research, ARS seeks to provide the means to solve the technical food and agricultural problems of broad scope and high national priority as required to ensure, perpetually, an adequate supply of high-quality food and fiber for the American people and for export.

ARS focuses on significant problems that are national in perspective in that they affect the entire Nation or its several broad geographic areas. The problems are sufficiently long range, high risk, and of such broad scope to require the unified planning, continuity of effort, and stable scientific environment maintained by a Federal research organization. They are not undertaken by other agricultural research institutions, because of their narrower geographic focus or shorter term perspective. The research is a uniquely Federal responsibility in that it is mandated by Congress for the Executive Branch and requires special skills, facilities, and capabilities and a structure ready to respond to emergency situations; is international, supporting foreign policy initiatives of the U.S. Government; maintains important national collections that are essential to scientific activities; and undergirds Federal action programs.

Biotechnology Research in the ARS Program Plan

The ARS Program Plan[4] is a description of all the research objectives and approaches planned for the Agency in the foreseeable future. The objectives of the plan are to "develop the means for—

1. Managing and conserving the Nation's soil and water resources for a stable and productive agriculture;

2. Maintaining and increasing the productivity and quality of crop plants;

3. Increasing the productivity of animals and the quality of animal products;

4. Achieving maximum use of agricultural products for domestic markets and export;

5. Promoting optimum human health and well-being through improved nutrition and family resource management; and

6. Integrating scientific knowledge of agricultural production, processing, and marketing into systems that optimize resource management and facilitate transfer of technology to users."

The agriculturally related biotechnologies can be applied to all parts of the ARS Program Plan. They are just one scientific method of attacking important problems.

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[4]Agricultural Research Service Program Plan, U.S. Department of Agriculture Miscellaneous Publication 1429. 1983. 73 pp.

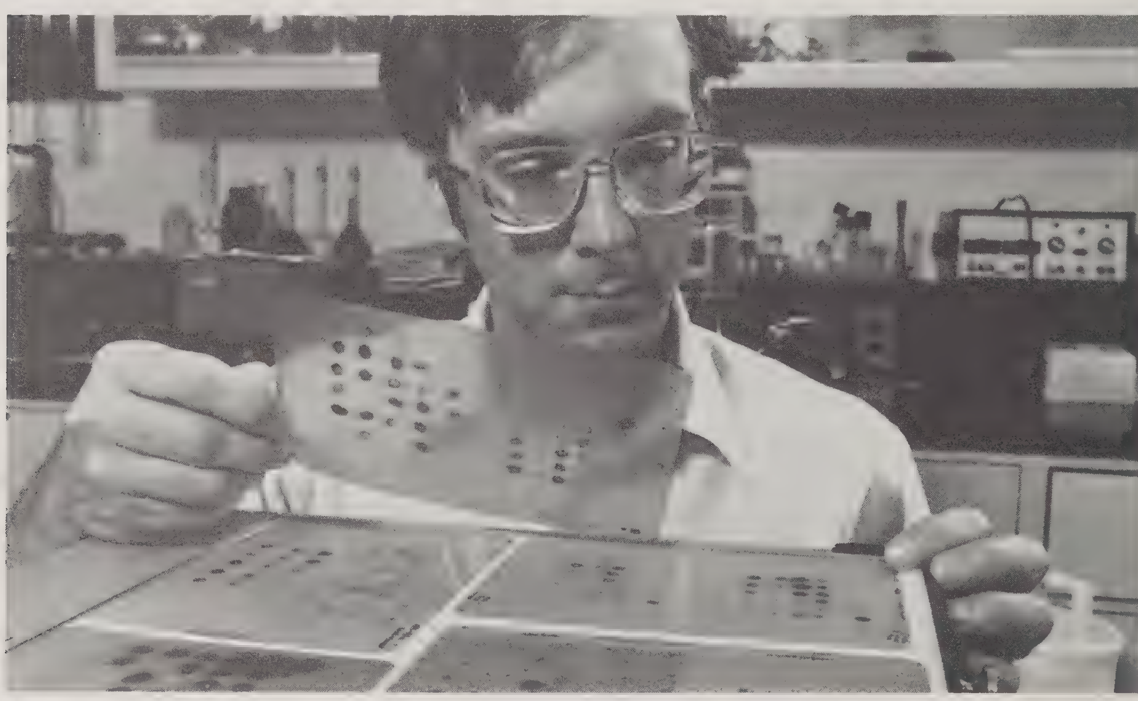
A Study to Determine How Best to Accelerate Biotechnology Research at Beltsville

Background and Purpose of the Study

In this great broad field of biotechnology, we needed to identify the thrusts that should be strengthened in the Beltsville Area or new thrusts that should be initiated. A finite and nearly constant source of funds, a limited number of scientists, and our current facilities were all that were available. We needed to identify a portion that we could tackle. In those areas that we did tackle, we wanted to become leaders. Groups of scientists of international distinction would form centers of excellence at Beltsville. So we undertook a study to accomplish these objectives.

The study concentrates on how scientists at Beltsville can solve important long-term agricultural problems using modern biotechnologies. Scientists will use their many talents in the conduct of research to solve these problems.

A great deal of important research that is not biotechnology related is conducted in the Beltsville Area. It is high quality and uses modern tools. It may, for example, be essential for some control or eradication program on which our agricultural productivity depends. This report focuses on only one aspect of Beltsville research—biotechnology as we have defined it. It does not address all the research in the Beltsville Area.



Detecting genes of viroids that infect potatoes. Researchers at Beltsville made a radioactive mirror-image copy (called cDNA) of the viroid's RNA, cloned it in *E. coli* bacteria, and incubated it with spots of potato juice on a piece of paper. The radioactive cDNA combined (hybridized) with spots on the paper containing the viroid RNA and washed out of spots not containing it. The radioactivity exposed the photographic film placed against the paper. (0681W628—28A)

Methods Used to Identify Areas to Study

Beltsville scientists volunteered to serve on task forces that developed eight background papers. In the papers summarized in the following section, the scientists identified the agricultural biotechnology-related opportunities at Beltsville. The sequence of these papers is from molecular to organelles, to cells, to organisms, and then to populations. Next, a summary was made of the thrusts identified by the scientists. Of these, the leaders at Beltsville identified three (and six subthrusts) for emphasis. These are described on pages 10 to 17.

Research Opportunities

What Genes Are and How They Work

We know that a gene is like a paragraph giving instructions in a foreign language for making one part of an organism. The language consists of three-letter words employing a four-letter alphabet. The words and necessary punctuation are strung together in long chains to form the paragraph. Many paragraphs are in one chapter or chromosome. And many chapters form the entire instruction book. A common language is used for all organisms, including plants, animals, and humans. The 3-letter words encode the 20 different amino acids that make up the functionally active parts of the organism. Sentences or paragraphs of the instructions can be snipped out of one organism and inserted into another.

We need to be able to identify the genes or paragraphs that give instructions for agriculturally important characteristics. We need to determine how the expression of the genes is controlled. We can then modify the genes or transfer them from one organism to another. We can use recombinant DNA techniques (recombining in one organism the genes for different functions derived from one or more organisms) to produce new, improved characteristics. In this way, we can modify and improve the productivity or disease resistance of the organism and thereby increase the efficiency of agricultural production.

How Genes Make Their Effects Known

Methods are available for injecting genes into animal cells or plant protoplasts. A few genes have been successfully transferred in this manner into mammalian, insect, or higher plant cells so that they have become a part of the genetic message of the recipient organism. We can detect the products of the genes. We need to know what controls the process of reading, translating, and implementing the instructions and what affects this control.

In the development of an animal, plant, or micro-organism, the instructions that are in the genes cannot be read and translated all at once. Some instructions must be read repeatedly from infancy through adulthood to old age, whereas others are read only in one stage and the reading must be turned off at other stages. A given message may be interpreted differently in various stages or in various organs of the organism. We need to know not only what the messages are, but how the reading of the messages is controlled and how the reading of one message affects another.

What Different Parts of a Cell Do

A cell has different parts, such as nucleus, cytoplasm, and membrane, just as the body of an animal has separate parts, such as head, liver, and skin. We know in a general way the function of some of the parts. For example, the genes that contain the instructions for making an organism are in the nucleus, and the parts that take in the "food" and convert it to the energy necessary for living are in the cytoplasm. We know that there are membranes that surround the nucleus and separate it from the cytoplasm, and we know there are many organs in the cytoplasm with special functions. We know that substances such as salts, water, oxygen, and sugars can penetrate these membranes.

We need to know what the role of the membrane is in moving these substances in and out of the cell and how this movement is controlled. On a larger scale, we need

to know what controls the development and maturation of plants and animals and what prevents some of them from developing in artificial culture media.

How Plants Take Up, Store, and Use Nitrogen From the Atmosphere

Nitrogen from the atmosphere supplies about one-half of that required for crop growth, and the rest comes from fertilizers. We know that plants cannot use the nitrogen in the air without the help of bacteria that absorb it from the air and convert it into proteins in their bodies. This protein then becomes available to the plant. There is a special relationship between the bacteria and the plant. We need to develop better plants and better bacteria so that more nitrogen can be converted into protein. Also, some bacteria release the nitrogen from fertilizers into the atmosphere, and we need to know how this can be prevented.

The nitrogen that is assimilated by the plant eventually finds its way into proteins that are stored in the seeds and that form the protein in the food for animals and humans. We need to know the genetic messages in the plant responsible for making these seed-storage proteins and what controls the reading and translation of those messages so that we can increase the amount of protein in the seeds that are our cereal grains.

Once the proteins are eaten, they are eventually reformed into our muscle proteins. We need to know what controls this reformation and what controls the proportion of muscle and fat.

Interactions Among Cells and the Groups of Cells We Call Organs

Cells are bounded by a very thin envelope composed of fatty materials and proteins that we call a membrane. Many little organs within a cell are bounded by or composed of membranes. These membranes have many different functions. They play a large role in capturing the energy from light and converting it and water and carbon dioxide from the air into carbohydrates through the process called photosynthesis. Beneficial substances, like nutrients, and harmful substances, like pesticides, penetrate the membranes. Substances that leave the cell, such as antibodies and hormones, have to leave by way of the membrane. Functions of the membrane are affected by a wide array of factors, such as diseases, toxins, heat, and cold. We need to know exactly how membranes are made and how they work. We need to know what controls their workings and how to affect these controls so that we can prevent the adverse effects of factors such as heat and cold and increase the beneficial effects such as the capture of light in photosynthesis.

Chemical Communication Among Cells and Organs

As animals or plants grow, their different parts grow in proportion. Each part depends on another; for example, in plants, leaves depend on roots for absorbing water, and, in animals, muscles depend on the mouth for taking in food. To operate as a whole, the various cells and organs in the body must communicate with one another. They use chemical messengers such as hormones and antibodies. Hormones produced at one site affect a cell or organ at another site. Antibodies produced by certain cells attack invading disease-causing organisms. We have only identified a few

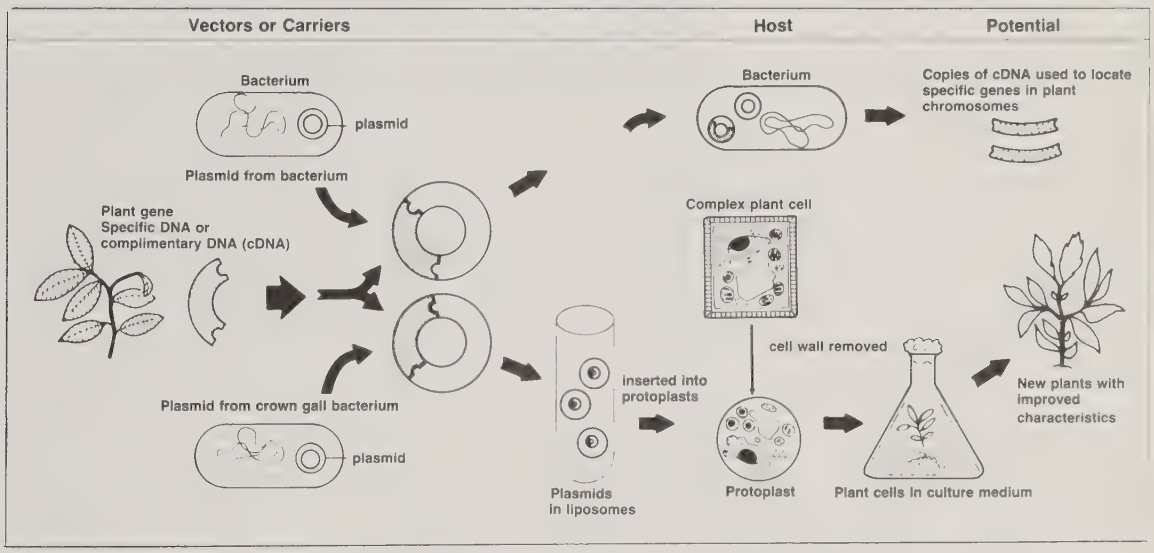
of these messengers, and we need to discover more of them and how they work. If we could control them, we could affect the way animals and plants grow and reproduce and how they resist disease.

Interactions Among Plants, Animals, and Microbes

Plants and animals live in an environment with millions of microbes. Some microbes are beneficial in helping plants and animals acquire and use nutrients. Other microbes are harmful and produce disease. We understand how some of these microbes produce their effects, although most interactions need to be investigated. We need to be able to manipulate these interactions to improve the beneficial effects and decrease the adverse effects. So we need to be able to enhance the resistance of both plants and animals to diseases. We also need to grow and modify the disease-causing organisms so that they are no longer harmful.

How Plants and Animals Withstand Changes in Their Environment

The growth of crops is often limited by factors in their environment such as lack of moisture, wrong temperature, or imbalance of nutrients. We need to understand the interactions between living things and their environment. We need to be able to modify plants and animals so they grow better in their natural environments, and we need to know how to modify their natural environments so that the plants and animals grow and produce at their maximum ability. Sometimes these interactions can be studied through artificial culture, and sometimes mathematical models can help us predict how the interactions work.



Gene transfer (manipulation) to improve crop plants. At left and upper right of diagram, recombinant DNA technology is used to locate a specific gene on a particular chromosome. At lower right, a plasmid (ring of genetic material) from a crown gall bacterium is used to transfer a plant gene found by this technique.

Choosing What Is Most Appropriate

From the potential universe of research opportunities previously described, leaders at Beltsville chose projects that fit the mission of ARS; that involve the newly developed methods and techniques; and for which Beltsville has scientists with the right kind of knowledge and land, buildings, and equipment to conduct the research with. Alternatively, these resources are available at nearby institutions that are willing to cooperate with us.

Our thrusts deal with research that is not being conducted elsewhere in ARS and in which Beltsville can establish itself as a leader. These thrusts had to fit the ARS 6-year program plan[5] and the priorities of the research staff scientists. They also had to look interesting and exciting and have the ability to draw others into cooperating in the research. In addition, they had to have a potential for something practical and useful.

The Research Agenda and the Current Research Program

Of the many thrusts that we identified as possible research material, we selected three major thrusts and six subthrusts. They are as follows:

Thrust A.—Genes. Characterize and Manipulate Biologically Important Genes and Their Products

Subthrust A-1: Modern Methods for Taxonomy and Germplasm Evaluation

We identify different life forms such as crop plants, seeds, weeds, insects, worms, bacteria, and viruses by their physical characteristics; that is, their appearance. Use of modern techniques, such as differences between enzymes or the genes themselves, could greatly facilitate our ability to identify and evaluate different life forms. We need to develop rapid methods to classify organisms, particularly harmful organisms that could cause severe damage to our crop plants and animals.

At Beltsville, scientists are taking the following approaches:

- Developing chromosome-handling techniques, studying cytogenetics, and examining isozymes. This research has been conducted on wasps that parasitize insects and on animal helminth parasites. These techniques will allow us to identify the parasites accurately, determine their evolutionary and ecological relationships, and develop biocontrol agents for insect pests and animal parasites.

Subthrust A-2: Manipulation of Genes of Economically Important Organisms

At Beltsville, scientists are taking the following approaches:

By identifying and manipulating the genes for converting atmospheric nitrogen into protein, we might be able to improve the process called nitrogen fixation. Also, we

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[5]Agricultural Research Service Program Plan. 6-Year Implementation Plan, 1984-1990. U.S. Department of Agriculture, Agricultural Research Service. Feb. 1983. 34 pp.

may be able to transfer the essential genes from plants capable of using atmospheric nitrogen into those not capable of doing so. Other genes for productivity could be transferred from different crops and animals.

- Determining the genes involved in nitrogen fixation in legumes, improving them, and then inserting them into grain crops. Determining the genes controlling the mutual recognition between plant and nitrogen-fixing bacterium and colonization of the plant nodule by the bacterium will permit enhancement of colonization and improve the growth of plants. Recombinant DNA methodology is being used to improve nitrogen fixation ability in legumes and to transfer this ability to grain crops and thereby reduce the need for nitrogen fertilizer.

- Introducing into soil bacteria the plasmids that control degradation of agricultural pesticides will reduce persistence of pesticides, prevent movement out of the root zone into the ground water, and provide a safe disposal system.

Plant cell culture and regeneration. White clumps (left) are cells forming from live wheat anthers; (center) masses of undifferentiated tissue grow from the cells; and (right), in a special growing medium, a small plant is regenerated from the cultured tissue. (0682X647—14A)

- Characterizing and manipulating the biologically important genes of soil micro-organisms will provide biological control agents for soilborne diseases and thereby reduce the need for pesticides and increase crop productivity.

- Applying plant cell and tissue culture techniques, such as anther culture and early stage embryo rescue. These techniques will greatly accelerate the development of important economic crops with better resistance to insects and diseases, increased yield, and a better balance of nutrients.

- Identifying and understanding the genes that control partition of nutrients and the synthesis of protein in seeds. Once identified, the genes can be altered to increase the amount of nutrients that go to storage organs such as seeds and taproots and therefore increase the protein content of the stored product.

- Developing improved methods for transferring genes from one plant to another, such as electrofusion of protoplasts and chromosome-mediated transformation. These techniques will allow the transfer of genetic information from one plant species to another.

- Identifying genes in micro-organisms that control production of microbial components that trigger resistance in plants. Insertion of these genes into saprophytes will be used as a tool in increasing the resistance of plants to disease agents.

- Identifying, isolating, and characterizing genes in micro-organisms by restriction-endonuclease mapping and hybridization. The organisms studied include arthropod viruses, bacteria that produce arthropod toxins, plant viruses, viroids, bacteriophages, and spiroplasmas. These studies will provide a better understanding of plant pathogens and improved methods of controlling disease organisms, including biocontrol of insects.

- Developing monoclonal antibodies to plant viruses and plant pathogens will advance studies of pathogen-host interactions, disease expression, and control.

- Developing methods for direct introduction of foreign genes into mammalian embryos will provide a new means for studying gene control and eventually will be used to control animal phenotypes at the molecular level and to increase growth and milk-production potential.

- Isolating parasite genes for the production of critical antigens and the insertion of these genes into "factory cells" for large-scale production of gene products will improve diagnostic tests and vaccines for animal parasites.

- Creating monoclonal antibodies that identify specific immune-system gene products is a major step toward locating and characterizing genes that affect and that can be used to control resistance to diseases such as mastitis.

- Isolating X- and Y-chromosome-bearing sperm using flow cytometry will enable development of a practical method to sex semen and to produce offspring of the desired sex, such as female dairy cattle.

- Elucidating the specific gene structure, expression, and molecular mechanisms of action of germination promoters and inhibitors will lead to better control of and rates of germination.

Thrust B.—Membranes. Determine the Structure, Function, and Regulation of Membranes

Subthrust B-1: Structure, Function, and Regulation in Membranes

We are working on the structure of plant and animal membranes and how herbicides and insecticides affect them, what causes ripening, how to prevent injury to membranes on freezing, and the unique structures on membranes of parasites.

At Beltsville, scientists are taking the following approaches:

- Identifying the types of environmental stress that alter membranes biochemically and anatomically will reveal ways of preventing membrane damage due to environmental stress.

- Understanding the action of oxidants on plant-membrane antioxidant systems and of substituted pyridazinones that alter fatty acid composition of plant membranes will permit an improved understanding of how these compounds regulate membrane function. Controlling membrane function will reveal ways to prevent the damaging effects of these compounds on plants.

- Studying the role of light and other environmental factors on membrane function as mediated by hormones will provide a better understanding of how the plant apportions carbohydrates among different organs.

- Controlling photosynthate partitioning may increase crop yield. Also, altering plant hormone control of transport of metabolites through membranes could enhance crop productivity.

- Understanding how membranes control penetration, absorption, and translocation of herbicides and bioregulators through themselves and through tissues and plant systems will allow the development of more effective and specific herbicides and bioregulators.

- Understanding the structure and function of membrane/cell wall components and the genes that control these components is a key step in understanding maturation, ripening, and senescence. Controlling senescence will improve the quality of fruits and vegetables.

- Determining the influence of sperm-membrane composition on fertilization will serve as a basis for creating a model system for studying membrane receptors and membrane fusion. Altering the receptors and improving fusion will lead to an increase in fertilization rate and thereby to the number of offspring from domestic animals.

- Understanding the roles of cell-surface receptors to hormones that regulate lactation and metabolism is central to devising means to improve efficiency of production.

- Using monoclonal antibodies to study antigens on parasites and receptors on host membranes will permit an understanding of how the parasites penetrate the host and cause disease and how the host resists the parasite. Genetic-engineering techniques are being used to produce antigens of parasites. These are the first steps in developing immunologically based disease-control procedures.

- Determining how parasites affect nutrient absorption and metabolism at the membrane level will lead to procedures for reducing the changes that cause production losses.

- Discovering the structures and mechanisms of transport for neuroactive peptides and neurotransmitters across membranes of insects is a prerequisite to developing strategies for control of those insects that affect animals, humans, and crop plants.

Thrust C.—Mediators. Isolate, Characterize, and Elucidate Mechanisms of Action of Chemical Mediators or Cell-to-Cell Communicators and Determine How Organisms Regulate Them

Subthrust C-1: Mechanism of Immunity

We are identifying the role of different cells and different antibodies in resistance to diseases and parasites. Findings from this research may enable us to develop new diagnostic tests and vaccines that enhance the ability of animals to resist disease.

At Beltsville, scientists are taking the following approaches:

- Using monoclonal antibodies in enzyme-linked immunosorbent and immunofluorescence assays will identify how certain bacteria damage the intestines of some farm animals but not others. Understanding how some farm animals resist colonization by these bacteria may permit development of techniques to prevent disease in all animals.

- Identifying differences in populations of lymphocytes and identifying how these cells communicate with one another will lead to methods of potentiation and stimulation of host response to infection and thus heighten protection against disease.

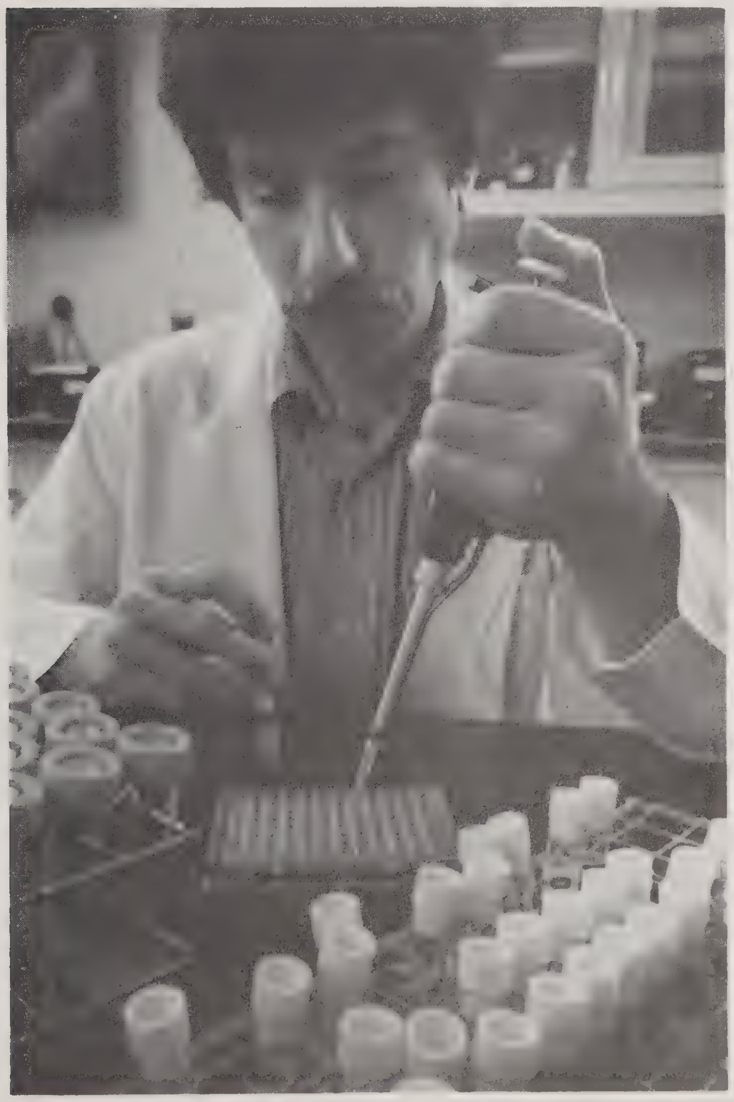
- Isolating and characterizing the mediators of clonal expansion of lymphocytes on exposure to parasite antigens will permit the use of these mediators to modulate protective immune responses and improve vaccination strategies.

Subthrust C-2: Mechanism of Interorgan Communications

We have just started studying the role of hormones in insects and worms. These hormones affect molting and reproduction. Applying the new technology will help speed the development of methods to control these pests.

At Beltsville, scientists are taking the following approaches:

- Developing monoclonal antibodies to specific metabolites will give sensitive probes to identify, localize, and quantify these metabolites in growth, development, and senescence. Finding ways to alter these metabolites will allow the development of more productive plants.



Immunity to animal parasite infections. Adding reagents to 96-well plate (equivalent to 96 test tubes) to test pig serum for trichinosis. A product of monoclonal antibody techniques, the test was developed at Beltsville as a tool for studying the mechanism of immunity, but it can be automated and adapted for commercial use in meatpacking plants. (0484X443-18A)

- Developing methods for regeneration of plants from tissue culture cells will permit the application of gene transfer technologies and greatly accelerate plant improvement.

- Measuring and understanding the mode of action of plant growth regulators such as brassino-steroids and the use of synthetic substitutes of regulators will allow the control of plant functions such as germination, flowering, fruit retention, growth, maturation, and senescence. Application of these substances can significantly increase yield, shorten time to harvest, and prevent deterioration after harvest.

- Isolating and identifying neurotransmitters, neuropeptide hormones, and other hormones will permit an understanding of the role of these mediators in insect development, behavior, and reproduction. This will permit the development of new strategies for insect control that are safe for the consumer and the environment.

- Using cell-culture techniques to study the neuroendocrine control mechanisms of pituitary peptide hormones and isohormones that regulate growth, reproduction, and metabolism of animals. This will allow the development of methods to increase growth rate and number of offspring per animal.

- Isolating and understanding how biochemicals of embryonic and endometrial origin that are involved in embryonic survival will permit the development of strategies to reduce embryonic deaths. It will also improve the techniques for manipulation and transfer of mammalian embryos.

- Investigating the hormonal control of tissue senescence (for example, how ethylene mediates membrane control of cell function in ripening) will lead to techniques to improve fruit quality and storage.

- Determining how the diet controls peptide hormone receptors on isolated liver, fat, and red blood cell membranes will explain how nutrients can influence glucose tolerance in experimental animals and humans.

- Determining how dietary fatty acids control the production of eicosanoid hormones in tissue culture and intact animals will permit an understanding of how hormones modulate cellular interactions in inflammatory and other reparative processes required for health in humans and farm animals.

Subthrust C-3: Mechanism of Communication Among Organisms

We have shown that the chemicals given off by a worm or insect will affect others of the same kind. Applying modern technologies, we can identify the chemicals that modify the behavior of worms and insects and speed the development of control technologies.

At Beltsville, scientists are taking the following approaches:

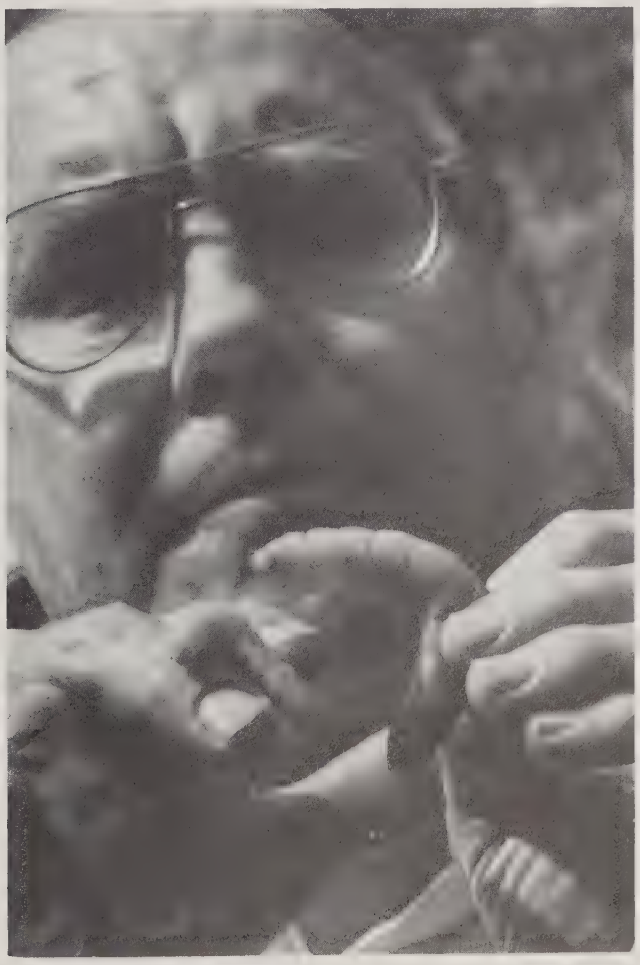
- Isolating and identifying chemicals from nematodes and from plants that modify nematode behavior will permit the better understanding of how these chemicals affect reproduction, aggression, dormancy, and migration of nematodes, particularly parasitic nematodes. This knowledge will permit the development of new methods to control nematode pests of crops.

- Characterizing and identifying olfactory receptors and understanding nerve-impulse patterns could provide the basis for developing antagonists that could be used to control insects.

- Characterizing and identifying the neurohormonal chemical mediators involved in pheromone production, understanding the conditions under which they are produced, and determining their mode of action could provide techniques to prevent pheromone production. Preventing pheromone production would result in the control of insects by interfering with reproduction.

Current Level of Effort

Currently, Beltsville employs about 37 scientists and a budget of about $6,260,000 on the new biotechnological thrusts. These figures represent between 8 and 9 percent of all resources in Beltsville.



Hormones that induce molting. Hormones produced by one organ of the body affect other organs. By blocking the pathway by which insects synthesize molting hormones from plant-derived sterols, a Beltsville scientist stunted the growth of the tobacco hornworm on the left. (0684X852—16)

In general, we have both the primary resources, such as scientists, buildings, and equipment, and the secondary resources, such as herbaria, collections, and animals, to do this work. In addition, we have a unique cooperation among scientists from various Federal and State laboratories, universities, and industries in the Beltsville vicinity and throughout ARS (see appendix A). Usually, no similar research is being conducted elsewhere in the Agency, and, where such research is being done, it complements that at Beltsville.

Strategies to Strengthen Research Activities

We have identified research thrusts that are the most pertinent and appropriate for the Beltsville Area. We plan to use every means possible to strengthen those thrusts. We will seek additional funds to strengthen those areas. Projects that are completed or projects that are not making progress will be closed out and their resources redirected to those thrusts. We will use every possible resource and flexibility to support those thrusts. We will also take every step possible to ensure the excellence of the research we are conducting.

Control of sex pheromone production. In tests done at Beltsville, researchers found that homogenized extract of brains of corn earworm injected into ligated females triggered sex pheromone production. This research revealed that a hormonal substance from the brain controls production of the sex pheromone used by the female to attract and sexually activate a mate. (0684X768—17A)

Appendix A: Unique Strengths of the Beltsville Area

One of the strengths of the Beltsville Area is its major concentration of Ph.D.-level scientists trained in the diverse disciplines of the biological and physical sciences that support the agricultural research community. At Beltsville, there are over 400 research scientists representing such disciplines as chemistry, plant physiology, plant pathology, genetics, virology, entomology, engineering, nutrition, parasitology, and soil science.

Another strength of the Area is its vast number of unique collections of germplasm and specimens of insects, fungi, seeds, rhizobia, and parasites that are used as reference materials for biological investigations. These collections are invaluable from both a national and international scientific perspective.

A third element is the facilities and equipment, at a single location, that are devoted totally to research. This includes a significant investment in scientific instrumentation and specialized research facilities.

A fourth consideration is location. Beltsville is in an invigorating scientific environment with other educational and research facilities such as the U.S. Department of Agriculture's National Agricultural Library; the University of Maryland; Johns Hopkins, Howard, Georgetown, and George Washington Universities; and other major Federal scientific laboratories such as the National Institutes of Health, the NASA-Goddard Space Flight Center, Food and Drug Administration, Walter Reed Army Medical Center, and U.S. Naval Research Laboratory. These scientific and educational institutions are superb sources of expertise in the physical and biological sciences that complement the agricultural research capabilities of the Area. The location of Beltsville near the Nation's Capital also provides considerable visibility to the agricultural research programs of USDA. Congressmen get a convenient look at the research programs, and a host of prominent international visitors tour the facilities annually.

Special Programs in the Beltsville Area

In addition to its fundamental research mission, the Beltsville Area has responsibility for some unique collections and other special programs important to the scientific and technological supremacy of American agriculture. Selected examples include:

1. U.S. National Parasite Collection. One of the largest collections of parasites in the world. It includes over 800,000 collection records and serves as a necessary working tool for research on parasites of animals and man throughout the world.

2. Index-Catalogue of Medical and Veterinary Zoology. An indepth index to the world's literature on parasites of animals. Computerization of the Index-Catalogue is nearing completion. This is an important working tool for all phases of parasitology research.

3. USDA Nematode Collection. A collection of over 23,000 cataloged slides and vials with specimens from worldwide sources, including over 14,000 species

entries and type specimens of about 1,000 species. Widely used by scientists in the United States and other countries to resolve nomenclature problems and investigate nematode hosts, occurrence, and distribution worldwide.

4. U.S. National Fungus Collections. The world's largest herbarium of fungus specimens, together with technical reference literature and data files. Accessions include over 800,000 collections, 100,000 taxa, and 25,000 types. Serves as a base for mycological research, principally research in the taxonomy of plant pathogens.

5. USDA Rhizobium Collection. A large and permanent collection of *Rhizobium* germplasm for research on the mechanism of nitrogen fixation by legumes. It is one of the largest public collections of *Rhizobium* in the world and has been maintained by USDA since 1912. Research and evaluation of *Rhizobium* strains are carried out in the laboratory, greenhouse, and field. Over 1,100 strains are identified and cataloged. The collection provides a safe depository of germplasm that is available internationally for all interested workers and research purposes, including the training of scientists from less-developed countries in techniques of rhizobiology. The collection is recognized as a component of Microbiological Resources Centers (MIRCENS) and is strongly supported by the U.S. Agency for International Development.

6. USDA National Small Grains Collection. A working inventory of germplasm of wheat, rice, barley, oats, and rye from countries around the world. About 85,000 accessions are maintained. Approximately 100,000 samples are exchanged annually with cooperators within the United States and about 50 other countries.

7. U.S. National Seed Herbarium. The world's largest taxonomic seed collection, including 90,000 seed-fruit samples and 25,000 species. Provides research material and references that can be used for rapid identification of isolated seeds and fruits of economically important plants.

8. U.S. National Entomological Collection. The largest holding of agriculturally important insect species in the Western Hemisphere. The collection of over 24 million specimens is a cooperative endeavor of USDA and the Smithsonian Institution. Specimens serve as a critical resource for research in most fields of entomology and are important for identification of insect pests.

9. ARS Biological Control Documentation Center. A central location where scientists in USDA and in other Federal, State, or private organizations can document and retrieve information on the releases of exotic beneficial arthropods in the United States.

10. USDA Hormone Program. Provides for the acquisition, characterization, and distribution of pituitary hormones and other endocrine-related reagents important to basic research in reproduction and animal physiology.

11. National Cooperative Dairy Herd Improvement Program. A cooperative effort involving dairymen in all 50 States, artificial insemination organizations, breed associations, USDA, and dairy-records processing centers. ARS provides technical coordination and uses nationwide data to develop scientific principles for improving the economically important genetic traits of dairy cattle.

12. USDA National Foundation Seed Project. A special project under which seeds from public varieties of grasses and legumes are annually produced in areas that are suitable for production of high-quality seeds. These seeds, in turn, are made available through crop improvement associations to States where climate conditions are not conducive to the production of high-quality seeds. As an allied activity, the Beltsville Area also coordinates the Organization for Economic Cooperation and Development (OECD) Seed Schemes in the United States.

13. Principal Plant Introduction Office. National focal point for the introduction, documentation, initial distribution, and exchange of plant germplasm. Coordinates the quarantine, documentation, and detention nursery programs for the National Plant Germplasm System. Over 100,000 items were exchanged in 1982, involving 120 countries.

14. Germplasm Resources Information Network. A unified national information system for plant germplasm conservation and use. Assists curators, breeders, and other plant scientists with the development of modern information networks for sharing data on the genetic characteristics of seeds and vegetative materials in the National Plant Germplasm System.

15. Chemicals Coordination Program. National focal point for coordinating the acquisition of promising new compounds from public and private laboratories for use by ARS scientists. Has major responsibility for developing computer-assisted techniques to organize chemical, physical, and biological data in order to find relationships that will lead to better pest-control chemicals. Coordinated programs involving 34 industry laboratories and 54 ARS scientists in 1982.

16. Pesticide Impact Assessment Program. A special program through which ARS participates in the National Agricultural Pesticide Impact Assessment Program of the Federal Government. Provides for coordination and joint participation by ARS in the technical review and impact assessments of all agriculturally related pesticides announced by the EPA for "Rebuttable Presumption Against Registration."

17. U.S. National Arboretum Herbarium. A collection of over 500,000 cataloged herbarium specimens of the plants grown by agriculturists and used for taxonomic, nomenclatural, floristic, and historical research.

18. U.S. National Arboretum Plant Collections. A 444-acre repository of woody plants used for landscaping, including the world's largest collections of conifers, maples, viburnums, crabapples, boxwoods, daylilies, herbs, azaleas, dogwoods, camellias, wildflowers, narcissus, and Asian plants.

19. Narcotic Plants Program. The only place in USDA licensed to grow essentially all drug-producing plants and to possess and experiment with all illegal drugs. Eleven years of experience includes control of plants with chemicals, factors affecting drug profiles in plants, and biochemistry of living and harvested products with emphasis on cocaine, opiates, and marihuana.
20. Plant Quarantine Program. A high-isolation facility in Glenn Dale, Md., to which potentially beneficial plants can be brought for examination and testing prior to their use in agriculture in the United States. Also associated are the Plant Exploration Office and Plant Introduction Office, which coordinate explorations and introduction for the Nation.

Interaction of the Beltsville Area With Nearby Research Institutions

Beltsville Area scientists interact with the following multidisciplinary scientific institutions located within 1/2 to 1 hour's drive:

Universities—Maryland, College Park; Maryland, Baltimore County; Georgetown, D.C.; George Washington, D.C.; Catholic, D.C.; Howard, D.C.; Johns Hopkins, Baltimore; Uniformed Services University of Health Sciences, Bethesda, Md.

Federal centers—National Agricultural Library, Washington Computer Center, National Institutes of Health, Armed Forces Institute of Pathology, U.S. Naval Research Laboratory, U.S. Naval Medical Center, Walter Reed Medical Center, Environmental Protection Agency, Food and Drug Administration, Food Safety and Inspecticn Service, National Zoological Center, Patuxent National Wildlife Research Center, Goddard Space Flight Center, National Bureau of Standards.

Other institutions—Radiation Biology Laboratory, Rockville, Md.; Johns Hopkins Applied Physics Laboratory, Laurel, Md.; American Type Culture Collection, Rockville, Md.; Crop Genetics International, Dorsey, Md.; Red Cross Blood Laboratory, Bethesda, Md.; Smithsonian Institution, D.C.; National Research Council/NAS, D.C.; National Science Foundation, D.C.; Maryland Agricultural Experiment Station, College Park.

Strongest interaction occurs with the Maryland Agricultural Experiment Station (MAES) and the University of Maryland. About one-half of the 50 laboratories in the Beltsville Area have formal cooperative agreements with the MAES. Other laboratories interact with the university and the staff of the MAES on a more informal basis.

Private Sector Interactions With Scientists in the Beltsville Area

A wide range of private sector groups visit the Area each year. Even though we do not have a compilation of such interests, the following examples illustrate the nature of the private sector interests in programs at Beltsville:

1. Patent on antifeedant for boll weevils, licensed to Biosystems Research, Inc.

2. Patent for insect maturation inhibitors, licensed to Stauffer Chemical Co.

3. Patent on control of nematodes and helminths, licensed to Pennwalt Corp.

4. Patent on attractants for the yellowjacket wasp, licensed to Morgro Chemical Co.

5. Memorandum of Agreement signed with Hoffman-LaRoche, Inc.; Genex Corp.; and Vineland Laboratories to produce genetically engineered proteins for research on poultry coccidiosis.

6. Cooperation with scientists at BASF in Germany on synthesis of compounds that alter membrane lipids in plant cells.

7. Several industrial firms (Upjohn, Rohm & Haas, Microlife Technics, and Biosystems Research) have collaborated with the Soilborne Diseases Laboratory on the development of potential biocontrol agents.

8. Several instrument companies (Technicon, Neotec, and Dickey-John) manufacture instruments based upon a prototype initially developed at Beltsville.

There are numerous other cooperative efforts involving herbicides, pesticide degradation, environmental contamination by pesticides, sludge utilization, insect traps (physical rather than chemical attraction), environmentally enhanced pesticide degradation, ground-water quality, and others.

Unique Equipment Relevant to Thrusts in the Beltsville Area

In addition to some of the most advanced commercially available equipment in the world, the Beltsville Area has some unique pieces of equipment not duplicated elsewhere. The following are examples:

1. Agricultural equipment laboratory. Twenty controlled-growth cabinets have been built that permit the creation of environments where ultraviolet, infrared, and thermal radiation can be removed from or added back to visible radiation. Serves as a basis for studying the spectral responses of all organisms.

2. Energy metabolism unit. A unique facility for the measurement of energy metabolism of cattle. This facility makes possible the measurement of an animal's response to nutritional and physiological manipulation. The unit is composed of six chambers for measurement of respiratory exchange. Two of the chambers permit simultaneous measurement of radioactive carbon in respired air. Data collection and computation is automated through the use of a computer-controlled data-acquisition system.

3. Flow cytometer/cell sorter. This instrument is capable of analyzing and sorting individual cells that have been tagged with a fluorescence marker. A laser is used as a light source that allows several thousand cells to be analyzed per second. Data acquisition and analyses are achieved with a built-in computer.

4. Light microscopy with macro- and micro-spectrophotometry. This equipment provides a unique capability to conduct qualitative and quantitative cytochemical and histochemical procedures for measuring proteins, nucleic acids and other complex organic compounds, and pH of single cells or their organelles and membranes.

5. Human calorimeter. This room-sized computer-controlled chamber is the largest, most sophisticated calorimeter in the United States for the study of energy metabolism in human volunteers. It contains more than 16,000 heat sensors for direct calorimetry and a mass spectrometer for indirect measurement of exchanges of oxygen, carbon dioxide, nitrogen, and other gases.

Appendix B: Membership of Task Forces for Study

Overall Chairman and Author	H. G. Purchase, Special Scientific Adviser to the Area Director, Beltsville Area
Steering Committee	M. Christiansen, Chairperson, Plant Physiology Institute B. Endo, Chairperson, Plant Protection Institute R. Fayer, Chairperson, Animal Parasitology Institute W. Mertz, Director, Beltsville Human Nutrition Research Center
Institute Chairpersons, Directors, and Leaders	H. M. Cathey, Director, National Arboretum M. Christiansen, Chairperson, Plant Physiology Institute B. Endo, Chairperson, Plant Protection Institute R. Fayer, Chairperson, Animal Parasitology Institute J. Hilton, Chairperson, Agricultural Environmental Quality Institute W. Mertz, Director, Beltsville Human Nutrition Research Center A. Piringer, Chairperson, Horticultural Science Institute R. Schroeder, Acting Chairperson, Insect Identification and Beneficial Insect Introduction Institute L. Smith, Chairperson, Animal Science Institute A. Stoner, Chairperson, Plant Genetics and Germplasm Institute K. Tippett, Leader, Family Economics Research Group
Chairpersons and Cochairpersons of Teams	E. Berlin, Beltsville Human Nutrition Research Center A. B. Borkovec, Agricultural Environmental Quality Institute D. E. Cress, Plant Physiology Institute D. W. DeJong, Plant Genetics and Germplasm Institute H. N. Guttman, Beltsville Human Nutrition Research Center R. H. Miller, Animal Science Institute K. D. Murrell, Animal Parasitology Institute L. D. Owens, Plant Physiology Institute M. J. Paape, Animal Science Institute J. F. Parr, Agricultural Environmental Quality Institute C. Rexroad, Animal Science Institute R. L. Ridgway, Agricultural Environmental Quality Institute M. D. Ruff, Animal Parsitology Institute J. B. St. John, Agricultural Environmental Quality Institute R. L. Steere, Plant Protection Institute W. J. VanDerWoude, Plant Physiology Institute D. F. Weber, Plant Physiology Institute
Team Members	Teams consisted of more than 116 scientists who volunteered to participate.

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